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Primary Leiomyosarcoma of the Ureter

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We report the thirteenth case of primary leiomyosarcoma of the ureter, as well as a summary of previous cases. It is the first case reported to be studied by computer tomography and immunohistochemical procedure. Further evaluation included intravenous pyelogram, cystoscopy with retrograde pyelogram, cell block for cytology, and electron microscopy. Leiomyosarcoma is a very rare disease that is difficult to diagnose. It has a very poor 5-year disease-specific survival. © 1996 Wiley-Liss, Inc.

KEY WORDS: **smooth muscle, tumor, urinary tract**

INTRODUCTION

Leiomyosarcomas originating from the ureter are exceedingly rare. Most primary ureteral tumors are of uroepithelial origin (i.e., transitional or squamous cell carcinoma). Primary ureteral tumors represent approximately 1% of all neoplasms of the upper urinary tract [1,2]. Benign and malignant mesenchymal tumors represent less than 3% of all primary ureteral tumors [3]. Herein, we describe the thirteenth reported case of primary leiomyosarcoma of the ureter; review the radiologic findings, including computed tomography (CT) scan; pathologic findings, including electron microscopy; and summarize the previously reported cases in tabular form.

CASE REPORT

A 54-year-old white woman presented to an outside hospital with intermittent left flank and lower quadrant abdominal pain for 4 months, frequency of urination, and intermittent hematuria. She had a history of two previous urinary tract infections and a 20-pound weight loss over the preceding 12 months. There were no other constitutional symptoms or history of kidney stones. Her past medical history was significant for irritable bowel/diverticular disease, anxiety/panic attacks, a right breast biopsy for benign disease, tonsillectomy, and adenoidectomy. The physical examination was unremarkable except for left flank pain and intermittent hematuria.

RADIOLOGIC AND UROLOGIC EXAMINATION

An infusion nephrotomogram revealed a moderately high-grade left hydroureteronephrosis down to the mid-left ureter. The distal one-half of the ureter was not visualized on delayed films. A definite obstructing calculus could not be identified. There was no evidence of a left renal mass. The right kidney and bladder were unremarkable. The patient was treated conservatively for a presumed left ureteral calculus. She continued to have pain for 2 weeks and then presented for cystoscopy, left retrograde pyelogram, left ureteroscopy with ureteral brushing, left renal pelvic barbotage, bladder barbotage, and left stent placement. Left retrograde pyelogram demonstrated nonvisualization of a 2.5-cm segment in the mid-ureter with proximal dilatation. A scout film suggested an obstructing calculus in the aforementioned region. Left ureteral biopsy and ureteral washings on two occasions revealed distorted reactive urothelium, benign reactive fibroblastic proliferation of the lamina propria suggestive of scar, and reactive transitional cells, but no evidence of malignant tumor cells or high-grade dysplasia, respectively. Ureteroscopically, the stricture was obstructing with multiple smooth erythematous rounded lesions not papillary in nature. A triple-contrast CT study demonstrated normal functioning kidneys bilaterally with prominence of the left pelvis and dilation of the proximal left ureter. The ureteral stent created some artifacts that precluded evaluation for small stones. A slightly irregular increased density surrounding the dilated proximal left ureter was suggestive of inflammation. Neither a definite ureteral mass nor enlarged adenopathy was identified. The remainder of the CT scan was normal, except for a right extrarenal pelvis.

The patient was referred to Loyola University Medical Center for definitive treatment. The physical examination

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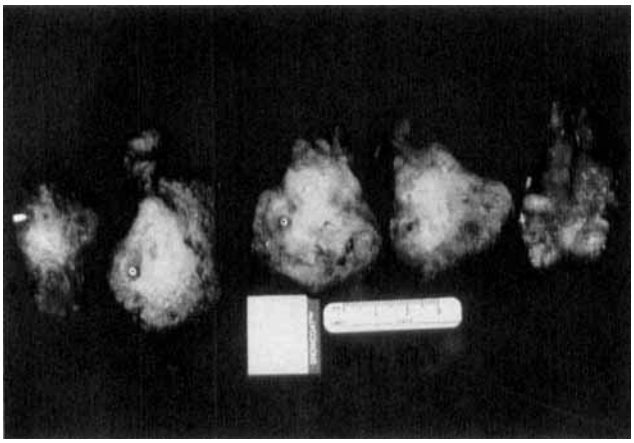

Fig. 1. Gross pathologic specimen of left ureteral leiomyosarcoma.

showed no changes, except for suprapubic tenderness. A mass was not palpated. Preoperative chest radiography and laboratory studies were normal, except for a triglyceride of 346 mg/dl. The urinalysis had 3+ protein, greater than 100 red blood cells, 2–5 white blood cells, and moderate bacteria.

The patient underwent laparotomy for exploration and repair of ureteral obstruction. Examination under anesthesia revealed a hard nodular mass (3 × 4 cm) on the left side of the abdomen that appeared to be at the level of the ureteral obstruction. A mid-line incision was made and the peritoneum was reflected in an attempt to perform the procedure extraperitoneally. A palpable mass was found within the sigmoid mesentery fixed to the aorta just above the external iliac artery. There were no other peritoneal abnormalities.

The ureter and left ovarian vein passed through the center of the mass. The left ovary, fallopian tube, and uterus were normal. The mass was dissected off the lateral aspect of the aorta, revealing the inferior mesenteric artery passing directly into the mass. The mass was mobilized by ligating the inferior mesenteric artery and completely dividing the large bowel mesentery circumferentially. The marginal artery of Drummond was intact. After ligation of the remaining attachments, ovarian vein superiorly, ureter superiorly, and inferiorly, the mass was excised with wide margins and sent for frozen section. The frozen section revealed a high-grade sarcoma, probably leiomyosarcoma. A left nephrectomy with adrenal preservation was performed because of the 4-to-6-cm ureteral defect and the diagnosis of high-grade sarcoma. The gross pathologic specimen revealed a 5.5 × 4.5 × 3.9-cm tan-yellow lobulated fibrotic upper left mesenteric mass entrapping the left ureter with stent and two vessels. The mass appeared to arise from the ureteral wall and extended both intraluminally and extraluminally (Fig. 1). The kidney was grossly and histologically normal, except for mild hydronephrosis.

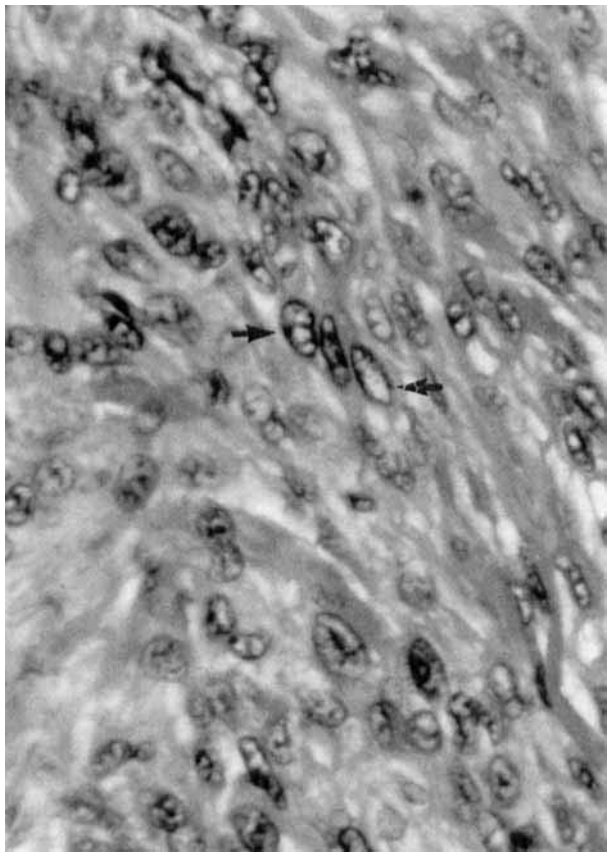

Fig. 2. Microscopic section of ureteral leiomyosarcoma. Note large spindle cells with cigar-shaped nuclei.

Microscopic sections of the mesenteric/ureteral mass revealed sheets of large spindle cells with cigar-shaped nuclei, many bizarre, large pleomorphic cells with hyperchromatic nuclei, and scant cytoplasm. An extremely high mitotic rate, more than 10 mitoses per high-power field, and atypical mitoses were present. The inked margins were free of tumor. Immunohistochemical studies revealed smooth muscle-specific actin and desmin as strongly positive and vimentin, S-100, and CD68 as negative (Fig. 2).

Ultrastructural examination via electron microscopy revealed a tumor composed of numerous mitoses, polymorphic and spindle-shaped cells containing fine cytoplasmic filaments of actin with rare interspersed fusiform dense bodies, most prominent in the periphery of the cell. The cytoplasm contained dilated cisternae of rough endoplasmic reticulum with fine and dense granular material (Fig. 3).

RADIATION ONCOLOGY FINDINGS

Six weeks postoperatively, the patient started a course of adjuvant radiation therapy. The treatment consisted of two courses of 10-MV photon, one AP and the other PA

Fig. 3. Electron micrograph of tumor cell showing elongated nucleus and bundles of myofilaments in the cytoplasm. Cisternae of dilated rough endoplasmic reticulum on the left of the nucleus. ×16,000.

of the left abdomen, followed by four courses of less penetrating energy, i.e., cobalt-60, for a total radiation dose of 50.4 Gy. Precautions were taken to exclude as much small bowel from the radiation field as possible. This was performed using a belly board during radiation to the left lateral field. The patient tolerated the procedure well with minimal diarrhea and no other significant acute side effects and actually gained 2.5 pounds.

POSTOPERATIVE FOLLOW-UP

At 9 months after the operation and neoadjuvant radiation therapy, the patient was doing very well clinically and was quite active in her daily routine. She had gained 15 pounds and complained of no gastrointestinal or genitourinary symptoms. Physical examination was within normal limits, with no peripheral lymphadenopathy or mass. CT of the pelvis and abdomen revealed no masses or lymphadenopathy. Thoracic CT scan uncovered a 1-cm stellate nodule at the apex of the right lung, suspicious of malignancy. There were multiple other nonspecific lung nodules and a lytic rib lesion. CT-guided biopsy with fine-needle aspiration was attempted without success, resulting in a pneumothorax requiring a chest tube.

A right thoracotomy with excision of pulmonary lesions revealed a high-grade sarcoma with extensive fibrosis. These lesions were morphologically similar to the ureteral leiomyosarcoma and consistent with metastasis.

DISCUSSION

Only 12 cases of malignant, smooth muscle neoplasms arising from the ureteral wall have been reported and this patient represents the thirteenth reported case. The first case was reported in 1943 by Rademaker [4]. The ureteral leiomyocarcinoma patients reported in the literature are summarized in Table I [4–15]. Their ages range from 34 to 79 years, with a mean of 58.4 and a median of 55 years. Most ureteral leiomyocarcinomas are found in females with a female-to-male ratio of 11:2. Presenting symptoms include flank/back pain in nine patients; four cases of gross hematuria, one urinary tract infection, four palpable masses, one hypertensive patient, and seven patients had a combination of the aforementioned symptoms. Radiographic examination included intravenous pyelogram (IVP), retrograde pyelogram, and CT. Eight patients received IVP: five revealed hydronephrosis, three with high-grade obstruction or nonfunction and 1 mass. The results of six retrograde pyelograms revealed total obstruction in four cases, displacement and compression in one, and stenosis in another case. Tumor size ranged from 1 to 12.5 cm, with mean size of 7.77 cm. This is the first case reported that has been studied by CT; unfortunately, the CT scan added no additional information as compared to the IVP or retrograde. One can only speculate as to the reason, but plausible explanations could be artifactual, created by the stent or overlying bowel and vessels in the triple-contrast study.

In retrospect, the slightly irregular increased density surrounding the dilated proximal ureter suggestive of inflammation was the ureteral leiomyosarcoma. This most likely would be better identified on CT scan, with no contrast or at most with IV contrast.

During surgical exploration, the differential diagnosis was of a mesenteric neoplasm invading the ureter or a retroperitoneal neoplasm encroaching on the ureter and mesenteric structure. Light microscopy immunohistochemical staining and electron microscopy were used to confirm the diagnosis of leiomyosarcoma. On gross cut examination, the mass was tan-yellow, lobulated, fibrotic (i.e., consistent with necrosis and hemorrhage) and had a whorled appearance characteristic of leiomyosarcoma. Immunohistochemical staining was positive for smooth muscle. Microscopically, the large spindle cells with cigar-shaped nuclei, increased frequency of mitosis, and bizarre pleomorphic cells differentiate this tumor from a benign leiomyoma.

The prognosis is unknown but is considered poor based on the limited number of case reports, with six patients dead within 2 years. Seven patients, including the current case, were reported to survive, but the length of follow-up is inconsistent: one alive with a follow-up of approximately 2 years, one alive after 5 months, one with no metastasis at surgery, one alive at 5 years, one with lung metastasis but alive at 5 years, one well at 2 months after surgery. Generally, leiomyosarcoma has a rapid growth with metastasis to mesentery, lung, liver, and regional lymph nodes. A better prognosis may be achieved if a complete margin-free resection is performed. Our patient was diagnosed with pulmonary metastasis to the right upper lobe and diaphragm via CT 9 months after surgery.

TABLE I. Review of Leiomyosarcoma of Ureter

Reference	Age/(Sex)	Symptoms/signs	Side	IVU	Retrograde	Tumor size (cm)	Comments
Rademaker (1943) [4]	59 (F)	Flank pain, palpable mass	L	Hydronephrosis	ND	12.5	No metastasis at surgery. Alive and well 14 months later.
Kraus (1994) [5]	48 (M)	UTI		ND	ND	10	Died of uremia and pneumonia. Autopsy: metastasis present.
Roosien and Russell (1946) [6]	55 (F)	Flank pain, palpable mass	R	ND	ND	9	Died of generalized metastasis 2 years later.
Zahorsky (1952) [7]	62 (F)	Flank pain, gross hematuria		ND	Stenosis	12	No metastasis at surgery. Alive and well 5 months later.
Alznauer (1955) [8]	60 (F)	Flank pain	R	No function	Total obstruction	3.5	Died of myocardial infarction 8 months later. Autopsy: metastasis widespread.
Werner et al. (1959) [9]	60 (F)	Flank pain	L	Hydronephrosis	Displaced and compressed	9	Died of multiple metastasis 6 months after surgery. No autopsy.
Hoger (1965) [10]	77 (F)	None	L	ND	ND	"Filbert"	Died of myocardial infarction. Autopsy: incidental finding of ureteral tumor.
Shah and Kothari (1971) [11]	60 (F)	Flank pain, palpable mass	L	Mass	ND	10	No metastasis at surgery.
Giraud and Rougé (1975) [12]	34 (F)	Hypertension	L	Hydronephrosis	ND	1	No metastasis at surgery. Alive and well 5 years later.
Roemer et al. (1980) [13]	79 (F)	Back pain, hematuria, palpable mass	L	Hydronephrosis	Total obstruction	5	No metastasis at surgery. Bone metastasis at 5 months; died at 15 months.
Werth et al. (1981) [14]	? (M)	NI	NI	NI	NI	NI	Metastasis to lung 1 year postoperatively, alive at 5 years.
Rushton et al. (1983) [15]	53 (F)	Flank pain, gross hematuria	R	High grade obstruction. No function at 24°	Complete obstruction	7 × 4 cm	Well at 2 months. Postoperatively treated with 4000 rads of radiation therapy.
Griffin and Waters (current case)	54 (F)	Flank pain, gross hematuria	L	Hydronephrosis obstruction	Nonvisualization; left ureter	5.5 × 4.5 × 3.9	Treated with 50.4 Gy postoperatively. Metastasis to right upper lobe of the lung and right diaphragm 9 months after surgery. Patient refused chemotherapy.

UTI, urinary tract infection; IVU, intravenous urogram; ND, not done; NI, no information

A right thoracotomy with excision of pulmonary and diaphragmatic masses confirmed the diagnosis of metastatic leiomyosarcoma of the ureter. The patient refused further medical treatment (i.e., chemotherapy) and remains alive 16 months after initial surgery.

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